AF/IFW 1646

PATENT
Customer Number: 22,852
Attorney Docket No: 03260.0047-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	)	
	)	
John Ernest SIMS	)	Group Art Unit: 1646
	)	
Serial No.: 09/612,921	)	Examiner: O. Chernyshev
	)	
Filed: July 10, 2000	)	Confirmation No.: 9162
	)	

For: IL-1 Delta DNA AND POLYPEPTIDES

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPEAL BRIEF UNDER 37 C.F.R. § 1.192

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GARRETT & DUNNER, L.L.P.

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Appellant appeals to the Board of Patent Appeals and Interferences from the Office Action mailed February 4, 2004, finally rejecting claims 58-62 and 65-67. The appealed claims are set forth in the attached Appendix.

Three copies of this Appeal Brief are being filed, along with the fee of $330.00 required under 37 C.F.R. § 1.17(c).

The Appeal Brief is due by August 3, 2004, and has been timely filed.

I. Real Parties in Interest

The real party in interest is Amgen Corporation, having purchased Immunex Corporation, the assignee.

II. Related Appeals and Interferences

There are currently no other appeals and no interferences known to the Appellant, the undersigned, or the assignee that will directly affect or be directly affected by or have a bearing on the Board's decision on this appeal.

III. Status of Claims

The application was filed on July 10, 2000, with claims 1-12, all of which were canceled in a Preliminary Amendment filed with the application. Claims 13-41 were added in the Preliminary Amendment.

Following a Restriction Requirement dated January 5, 2001, Appellant filed a Response on February 4, 2001, electing the claims of Group I (claims 13-24, 35, and 36). Following an additional Restriction Requirement dated March 8, 2001, Appellant filed a Response on April 9, 2001, again electing the claims of Group I (claims 13-24, 35, and 36) and specifying SEQ ID NO:3 for examination.

Claims 13-24, 35, and 36 were rejected in an Office Action dated July 30, 2001. In an Amendment and Response dated November 30, 2001, Appellant canceled claims 13-41 and added claims 42-57.

In an Office Action dated February 27, 2002, claims 42-57 were rejected. In an Amendment and Response dated August 27, 2002, Appellant amended claim 52.

Claims 42-57 were again rejected in an Office Action dated November 18, 2002. On February 19, 2003, Appellant filed a Notice of Appeal. On May 19, 2003, Appellant filed a Request for Filing a Continued Prosecution Application with an Amendment. In the Amendment, claims 42-57 were canceled and claims 58-78 were added.

Claims 58-78 were rejected in an Office Action dated June 26, 2003. In an Amendment and Response dated December 19, 2003, Appellant canceled claims 63-64 and 68-78 and amended claims 58, 62, and 65.

Claims 58-62 and 65-67 were again rejected in an Office Action dated February 4, 2004. Appellants filed a Notice of Appeal on June 3, 2004.

In Summary, claims 1-57, 63, and 64, and 68-78 have been canceled. Claims 58-62 and 65-67 have been finally rejected and are on appeal. No claim has been allowed.

A copy of claims 58-62 and 65-67 can be found in the Appendix.

IV. Status of Amendments

Appellant filed an Amendment on December 19, 2003, canceling claims 63, 64, and 68-78 and amending claims 58 and 62. In an Office Action dated February 4, 2004, the Examiner indicated that this Amendment has been entered.

V. Summary of the Invention

Appellant's invention must be viewed in light of the state of the art at the time the invention was made. At that time, patients with various rearrangements associated with the proximal long arm of chromosome 2 had been reported in the literature. For example, Mu et al. had reported that a patient suffering from numerous physical abnormalities had a tandem duplication of 2q11.2-q14.2. In addition, Glass et al. had reported that a mother and child suffering from numerous physical abnormalities had a proximal 2q trisomy (2q11.2-q21.1). That is, the patients had an insertion of chromosome 2-derived material into the middle of the short arm of chromosome 8. Thus, at the time that Appellant made his invention, it was appreciated in the art that a variety of rearrangements of the proximal arm of chromosome 2 were associated with physical abnormalities. It was further appreciated that a variety of hybridization techniques could be

used to analyze these rearrangements using probes mapping to the rearranged region. Appellant's invention provides such probes.

Appellant discovered the DNA sequence of the human IL-1 delta gene and that it mapped to the proximal long arm of chromosome 2. (Specification at 8 and 37.) Appellant found that all or part of human IL-1 delta gene could be used to identify human chromosome 2, and the specific locus thereof, that contains the DNA of IL-1 delta family members. (*Id.* at 37.) Thus, Appellant's gene provides a genetic marker for a specific region of chromosome 2. Appellant determined that the human IL-1 delta gene could be used as a probe in techniques such as radiation hybrid mapping, in situ hybridization to chromosome spreads, and Southern blot hybridization to hybrid cell lines containing individual human chromosomes. (*Id.*)

Appellant recognized that human chromosome 2 is associated with specific diseases including glaucoma, ectodermal dysplasia, insulin-dependent diabetes mellitus, wrinkly skin syndrome, T-cell leukemia/lymphoma, and tibial muscular dystrophy. (*Id.* at 37.) Thus, based on the chromosomal localization of the human IL-1 delta gene, Appellant asserted that all or part of the human IL-1 delta gene could be used to distinguish conditions in which this genetic marker is rearranged or deleted. (*Id.*) When viewed

in light of the knowledge in the prior art of the association of rearrangements of the proximal long arm of chromosome 2 with physical abnormalities, it is evident that all or part of the human IL-1 delta gene can be used as a probe for a specific region of chromosome 2 to analyze such rearrangements for diagnostic purposes.

Appellant is claiming isolated human IL-1 delta nucleic acids. (*See* Appendix).

VI. Issues

In this appeal, Appellant presents two issues to the Board for review:

1) whether the invention of claims 58-62 and 65-67 has a specific, substantial, and credible utility as required by 35 U.S.C. § 101. This same issue is also expressed by the Office as whether the skilled artisan would know how to use the invention of claims 58-62 and 65-67 as required by 35 U.S.C. § 112, first paragraph; and

2) whether the invention of claims 60, 61, and 65-67 is sufficiently described in Appellant's specification as required by 35 U.S.C. § 112, first paragraph.

VII. Grouping of Claims

For purposes of appeal, the claims are grouped as follows, and will be argued accordingly.

With respect to the appealed grounds of rejection of claims 58-62 and 65-67 for lacking a specific, substantial, and credible utility under 35 U.S.C. § 101, and for failing to disclose how to use the claimed invention under 35 U.S.C. § 112, first paragraph, the claims stand or fall together.

With respect to the appealed grounds of rejection of claims 60, 61, and 65-67 for lacking an adequate written description, claims 60 and 61 stand or fall together and claims 65-67 stand or fall together.

VIII. Argument

A. Appellant's human IL-1 delta DNAs have a specific, substantial, and credible utility

Claims 58-62 and 65-67 recite isolated human IL-1 delta nucleic acid molecules. Appellant's specification asserts a number of utilities for human IL-1 delta nucleic acid molecules. One of those utilities is the use of the claimed nucleic acid molecules as a genetic marker to distinguish conditions in which the human IL-1 delta gene on the proximal long arm of chromosome 2 is rearranged or deleted. Appellant will show that this utility is a specific, substantial, and credible utility.

1. The specification asserts a utility for human IL-1 delta DNAs

The specification asserts a number of utilities for IL-1 delta DNA. One of those asserted utilities, on which Appellant will focus this Brief, is the use of human IL-1 delta DNAs as a genetic marker to distinguish conditions in which the human IL-1 delta DNAs on chromosome 2 is rearranged or deleted:

> As set forth above, **SEQ ID NO:3 has been mapped to the 2q11-12 region of chromosome 2.** Human chromosome 2 is associated with specific diseases which include but are not limited to glaucoma, ectodermal dysplasia, insulin-dependent diabetes mellitus, wrinkly skin syndrome, T-cell leukemia/lymphoma, and tibial muscular dystrophy. Thus, **the nucleic acid of SEQ ID NO:3, or a fragment thereof, can be used by one skilled in the art using well-known techniques to analyze abnormalities associated with gene mapping to chromosome 2. This enables one to distinguish conditions in which this marker is rearranged or deleted.** In addition, nucleotides of SEQ ID NO:3 or a fragment thereof can be used as a positional marker to map other genes of unknown location.

(Specification at 37, lines 24-32, emphasis added.) The specification also describes some of the well-known techniques that can be used with this genetic marker to detect rearrangements of the human Il-1 delta gene:

> Human IL-1 delta gene maps to chromosome 2q11-12. All or a portion of the nucleic acids of SEQ ID NO:3, including oligonucleotides, can be used by those skilled in the art using well-known techniques to identify human chromosome 2, and the specific locus thereof, that contains the DNA of IL-1 delta family members. Useful techniques include, but are not limited to, using the

> sequence or portions, including oligonucleotides, as a probe in various well-known techniques such as radiation hybrid mapping (high resolution), in situ hybridization to chromosome spreads (moderate resolution), and Southern blot hybridization to hybrid cell lines containing individual human chromosomes (low resolution).

(*Id.* at 37, lines 2-9.) Thus, Appellant's specification asserts that human IL-1 delta DNAs are useful for distinguishing conditions in which the human IL-1 delta gene on the proximal long arm of chromosome 2 is rearranged or deleted. This utility is specific, substantial, and credible.

2. Appellant's asserted utility for human IL-1 delta DNAs is specific

All of Appellant's claimed nucleic acids have the property of being capable of specifically hybridizing to a particular region on chromosome 2. The specificity of this utility arises from the specific location of the human IL-1 delta gene on the proximal long arm of chromosome 2. (Specification at 37, lines 2-9; Declaration of John E. Sims submitted December 19, 2003, at ¶¶7-9.) Consequently, Appellant's asserted utility is specific.

The Office recognizes that human IL-1 delta DNA has a specific location on a specific chromosome. (February 4, 2004, Office Action at 3: "One skilled in the art readily recognizes that any naturally occurring DNA has a 'specific location' . . . on a specific corresponding chromosome.") Moreover, the Office

has admitted that one skilled in the art could use the claimed DNAs for *in situ* hybridization with a "specific site on human chromosome 2." (*Id.*) All polynucleotides would not be useful for the asserted utility. (Declaration of John E. Sims at ¶9.) It is indisputable that Appellant's asserted utility is specific.

3. Appellant's asserted utility for human IL-1 delta DNAs is substantial

Appellant's asserted utility that IL-1 delta nucleic acids can be used to distinguish conditions in which the human IL-1 delta gene is rearranged or deleted is substantial. Appellant localized the human IL-1 delta gene to chromosome 2q11-12. (Declaration of John E. Sims at ¶6.) As the specification asserts, human IL-1 delta nucleic acids can be used "to distinguish conditions in which this marker is rearranged or deleted". . ."using well-known techniques." (Specification at 37, lines 27-30.)

One well-known technique that is specifically described in the specification is "in situ hybridization to chromosome spreads." (*Id.* at 37, lines 7-8.) Thus, Appellant's specification indicates that human IL-1 delta nucleic acids can be used for *in situ* hybridization to chromosome spreads to distinguish conditions in which the human IL-1 delta gene is rearranged or deleted. (Declaration of John E. Sims at ¶6.)

Since the human IL-1 delta gene is localized to 2q11-12, the skilled artisan would have understood at the time that the application was filed that IL-1 delta nucleic acids could be used to distinguish conditions associated with rearrangements or deletions of 2q11-12. (*Id.* at ¶7.) This utility is substantial.

The substantial nature of this asserted utility is supported by objective evidence of record. (*Id.* at ¶¶4-6 and 11-20.) In 1984, a paper was published describing a condition associated with rearrangements or deletions of 2q11-12. Mu et al., *Journal of Medical Genetics*, 1984, 21:57-71. Mu et al. examined a patient with various abnormalities, and found an abnormal proximal long arm of chromosome 2. (Mu et al. at 57; Declaration of John E. Sims at ¶12.) The authors determined that there was a tandem duplication of 2q11.2-q14.2. (*Id.*) Similarly, Glass et al. published a paper in 1988 describing a mother and child suffering from numerous physical abnormalities had a proximal 2q trisomy (2q11.2-q21.1). Glass et al., *Journal of Medical Genetics*, 1988, 35:319-322. The patients had an insertion of chromosome 2-derived material into the middle of the short arm of chromosome 8. (Glass et al. at 320; Declaration of John E. Sims at ¶15.)

Based on Mu et al. and Glass et al., the skilled artisan

would have understood that IL-1 delta nucleic acids could be used for *in situ* hybridization of chromosome spreads from this patient to distinguish rearrangements or deletions of the human IL-1 delta gene. (Declaration of John E. Sims at ¶13 and ¶16.) That is, IL-1 delta nucleic acids could be used to determine the presence of normal chromosome 2 sequences on one of the chromosomes and for characterizing the duplicated region of the abnormal chromosome. (*Id.* at ¶¶13-14 and ¶¶16-17.) This is a "real world use." (*Id.* at ¶18.)

A substantial utility is one "that defines a 'real world' use." M.P.E.P. § 2107.01 at 2100-32, col. 2. Since Appellant's utility defines a "real world use," Appellant's utility is a substantial utility.

In addition, "any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a 'substantial' utility." M.P.E.P. § 2107.01 at 2100-33, col. 1. Appellant's use of IL-1 delta nucleic acids to distinguish rearrangements or deletions of the human IL-1 delta gene in patients should be viewed as providing a public benefit since the patient in Mu et al., as well as patients with a similar chromosomal and resultant physical abnormalities, would

benefit from diagnosis using Appellant's claimed nucleic acids. (Declaration of John E. Sims at ¶¶19-20.) Such diagnosis would identify the cause of the physical abnormalities exhibited by the patient, and would rule out other causes of the abnormalities. There can be no doubt that Appellant's asserted utility is substantial.

4. Appellant's asserted utility for human IL-1 delta DNAs is credible

The evidence of record shows that, as Appellant asserted in the specification, the claimed nucleic acids can be used to distinguish conditions in which the human IL-1 delta gene is rearranged or deleted. (Declaration of John E. Sims at ¶¶7, 10-11, 13-14, and 17-20.) The Office has provided no evidence to the contrary, nor even argued that this utility is not credible. In fact, the Office has conceded that "one skilled in the art could use the instant polynucleotides for *in situ* hybridization with a specific site on human chromosome 2 'without the need for any additional research' . . . ." (February 4, 2004, Office Action at 3-4.) In view of the evidence of record, the credibility of this utility is unquestionable.

5. Appellant's human IL-1 delta DNAs provide a specific benefit in currently available form

The claimed human IL-1 delta DNAs fulfill the requirements

for patentable utility set out by the Supreme Court in *Brenner v Manson*:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Appellant's human IL-1 delta DNAs have been refined and developed to a point at which they can be used without any need for any additional research. (Declaration of John E. Sims at ¶11.) Appellant provided the sequence for the human IL-1 delta gene, its chromosomal location, and a teaching to use the DNA to detect chromosomal rearrangements of a specific region of chromosome 2. No additional research is required to use the claimed nucleic acids.

The Office concedes that "one skilled in the art could use the instant polynucleotides for *in situ* hybridization with a specific site on human chromosome 2 'without the need for any additional research' . . . ." (February 4, 2004, Office Action at 3-4.) The Office conditions this concession, stating that "the instant nucleic acids could be used as specific markers for a certain abnormality only if a specific mutation in 2q11-12

region is disclosed as being associated with such an abnormality." (*Id.* at 4.) The Office's position ignores the skilled artisan's knowledge of rearrangements of this region, as illustrated by Mu et al. and Glass et al. When this knowledge is taken into account, the Office's position collapses.

Following Appellant's teachings, the skilled artisan could use IL-1 delta nucleic acids for *in situ* hybridization of chromosome spreads from patients to distinguish rearrangements or deletions of the human IL-1 delta gene. (Declaration of John E. Sims at ¶16.) For example, IL-1 delta nucleic acids could be used to determine the presence of normal chromosome 2 sequences and for characterizing the insertion of material derived from chromosome 2 into chromosome 8. (*Id.* at ¶¶17-18.) This utility for the claimed nucleic acids provides a specific benefit in currently available form. Thus, Appellant's claimed human IL-1 delta nucleic acids fulfill the Supreme Court's mandate in *Brenner v. Manson*.

6. Appellant's asserted utility fulfills 35 U.S.C. § 101 and 35 U.S.C. § 112

As Appellant has demonstrated above, the asserted utility that the claimed human IL-1 delta nucleic acids can be used to distinguish conditions in which the human IL-1 delta gene is rearranged or deleted is a specific, substantial, and credible

utility. The Board should reverse the rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph.

B. Appellant's specification describes the nucleic acids of claims 60 and 61

Claims 60 and 61 recite an isolated nucleic acid molecule comprising at least 30, or at least 60, contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:3. Appellant's specification provides the DNA sequence of human IL-1 delta DNA, SEQ ID NO:3. (Specification at 8.) The specification further describes:

> Among the uses of nucleic acids of the invention is the use of fragments as probes or primers. Such fragments generally comprise at least about 17 contiguous nucleotides of a DNA sequence. **In other embodiments, a DNA fragment comprises at least 30, or at least 60 contiguous nucleotides of a DNA sequence.**

(Specification at 36, lines 16-19, emphasis added.) When this passage is read in conjunction with Appellant's disclosure of the DNA sequence of SEQ ID NO:3, it is evident that Appellant had possession of the nucleic acids of claims 60 and 61 at the time that the application was filed. The Board should reverse the rejection of claims 60 and 61 under 35 U.S.C. § 112, first paragraph, for lacking an adequate written.

C. Appellant's specification describes the nucleic acids of claims 65-67

Claims 65-67 are dependent on claim 62, which was not

included in the rejection.[1] Claim 62 recites an isolated nucleic acid molecule that hybridizes to SEQ ID NO:3 under conditions of high stringency. Appellant's specification provides the DNA sequence of human IL-1 delta DNA, SEQ ID NO:3. (Specification at 8.) The specification further describes DNAs that hybridize to SEQ ID NO:3 under the stringent conditions recited in the claims:

> The invention thus provides isolated DNA sequences encoding polypeptides of the invention, selected from: (a) **DNA comprising the nucleotide sequence of** SEQ ID NO:1 or **SEQ ID NO:3**; (b) DNA encoding the polypeptides of SEQ ID NO:2 or SEQ ID NO:4; (c) DNA capable of hybridization to a DNA of (a) or (b) under conditions of moderate stringency and which encodes polypeptides of the invention; (d) **DNA capable of hybridization to a DNA of (a) or (b) under conditions of high stringency** and which encodes polypeptides of the invention, and (e) DNA which is degenerate as a result of the genetic code to a DNA defined in (a), (b), (c), or (d) and which encode polypeptides of the invention. Of course, polypeptides encoded by such DNA sequences are encompassed by the invention.
>
> * * *
>
> As used herein, conditions of moderate stringency can be readily determined by those having ordinary skill in the art based on, for example, the length of the DNA. The basic conditions are set forth by Sambrook et al. Molecular Cloning: A Laboratory Manual, 2 ed. Vol. 1, pp. 1.101-104, Cold Spring Harbor Laboratory Press, (1989),

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1 In an Office Action dated February 4, 2004, claim 65 was objected to as being in improperly dependent form for failure to further limit the subject matter of claim 62. After a telephonic interview with the undersigned (*see* February 24, 2004, Office Communication), the objection was withdrawn. Appellants respectfully note that claims 65-67 are properly dependent on claim 62.

> and include use of a prewashing solution for the nitrocellulose filters 5XSSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0), **hybridization conditions of about 50% formamide, 6XSSC at about 42°C** (or other similar hybridization solution, such as Stark's solution, in about 50% formamide at about 42°C.), and washing conditions of about 60°C., 0.5XSSC, 0.1% SDS. **Conditions of high stringency** can also be readily determined by the skilled artisan based on, for example, the length of the DNA. Generally, such conditions **are defined as hybridization conditions as above, and with washing at approximately 68°C., 0.2XSSC, 0.1% SDS**. The skilled artisan will recognize that the temperature and wash solution salt concentration can be adjusted as necessary according to factors such as the length of the probe.

(Specification at 11-12, emphasis added.) Thus, Appellant describes DNAs that hybridize to SEQ ID NO:3 under the claimed hybridization conditions. The Office has conceded this in that these limitations are included in independent claims 62, which was *not* included in the rejection on the ground of lacking an adequate description.

Claims 65-67 recite that the nucleic acid is at least 95%, 98%, or 99% identical to SEQ ID NO:3. Literal support for these limitations is found in the specification:

> In another embodiment, the nucleic acid molecules of the invention also comprise nucleotide sequences that are at least 80% identical to a native sequence. Also contemplated are embodiments in which a nucleic acid molecule comprises a sequence that is at least 90% identical, **at least 95% identical, at least 98% identical, at least 99% identical,** or at least 99.9% identical to a native sequence.

(Specification at 12-13, emphasis added.) When this passage is

read in conjunction with the rest of Appellant's disclosure, it is clear that Appellant had possession of the nucleic acids of clams 65-68 at the time that the application was filed. Appellant requests that the Board reverse the rejection of claims 65-68 under 35 U.S.C. § 112, first paragraph, for lacking an adequate written description.

IX. Conclusion

The rejection of claims 58-62 and 65-67 under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, on the grounds of lack of utility is in error. Reversal of the rejection is respectfully requested.

The rejection of claims 60, 61, and 65-67 under 35 U.S.C. § 112, first paragraph, on the grounds of lack of an adequate written description is in error. Reversal of the rejection is respectfully requested.

Please grant any extensions of time required to enter this Appeal Brief and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: _____
Salvatore J. Arrigo
Reg. No. 46,063

Date: August 2, 2004

APPENDIX

The claims on appeal are as follows:

58. An isolated nucleic acid molecule consisting of the nucleic acid sequence of SEQ ID NO:3.

59. An isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO:3.

60. An isolated nucleic acid molecule comprising at least 30 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:3.

61. The nucleic acid molecule of claim 60, wherein said nucleic acid molecule comprises at least 60 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:3.

62. An isolated nucleic acid molecule that hybridizes to either strand of a denatured, double-stranded DNA comprising the nucleic acid sequence of SEQ ID NO:3, wherein the hybridization conditions include 50% formamide and 6XSSC, at 42°C with washing conditions of 68°C, 0.2XSSC, 0.1% SDS.

65. The nucleic acid molecule of claim 62, wherein said nucleic acid molecule is at least 95% identical to the nucleic acid sequence of SEQ ID NO:3.

66. The nucleic acid molecule of claim 65, wherein said nucleic acid molecule is at least 98% identical to the nucleic acid sequence of SEQ ID NO:3.

67. The nucleic acid molecule of claim 66, wherein said nucleic acid molecule is at least 99% identical to the nucleic acid sequence of SEQ ID NO:3.